WAYNE A. SHAFFER (SBN 1519)
LAXALT & NOMURA, LTD.
9600 Gateway Drive
Reno, Nevada 89521
Tel: 775-322-1170
Fax: 775-322-1865
wshaffer@laxalt-nomura.com

ALAN B. CLEMENT (admitted *pro hac vice*)
LOCKE LORD LLP
Brookfield Place
200 Vesey Street, 20th Floor.
New York, New York 10281
Tel.: 212-415-8600
Fax: 212-303-2754
aclement@lockelord.com

MYOKA KIM GOODIN (admitted *pro hac vice*)
JENNIFER CORONEL (admitted *pro hac vice*)
LOCKE LORD LLP
111 S. Wacker Drive
Chicago, Illinois 60606
Tel: 312-443-0700
Fax: 312-443-0336
mkgoodin@lockelord.com
jennifer.coronel@lockelord.com

Attorneys for Defendants
West-Ward Pharmaceuticals Corp. and
West-Ward Pharmaceuticals International Limited

MICHAEL D. ROUNDS, Bar No. 4734
RYAN J. CUDNIK, Bar No. 12948
BROWNSTEIN HYATT FARBER SCHRECK, LLP
5371 Kietzke Lane
Reno, Nevada 89511
Tel: (775) 324-4100
Fax: (775) 333-8171
mrounds@bhfs.com
rcudnik@bhfs.com

CONSTANCE S. HUTTNER (admitted *pro*

JOHN P. DESMOND
Nevada Bar No. 5618
BRIAN R. IRVINE
Nevada Bar No. 7758
DICKINSON WRIGHT PLLC
100 West Liberty St., Suite 940
Reno, Nevada 89501
Tel: (775) 343-7500
Fax: (775) 786-0131
jdesmond@dickinsonwright.com
birvine@dickinsonwright.com

J.C. ROZENDAAL (admitted *pro hac vice*)
MICHAEL E. JOFFRE (admitted *pro hac vice*)
CHANDRIKA VIRA (admitted *pro hac vice*)
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue N.W.
Washington, D.C. 20005-3934
Tel: (202) 371-2600
Fax: (202) 371-2540
jcrozendaal@skgf.com
mjoffre@skgf.com
cvira@skgf.com

Attorneys for Defendant
Teva Pharmaceuticals USA, Inc.

hac vice)
CAROLINE SUN (admitted *pro hac vice*)
BETH FINKELSTEIN (admitted *pro hac vice*)
BUDD LARNER, P.C.
150 John F. Kennedy Parkway
Short Hills, New Jersey 07078
Tel: (973) 379-4800
Fax: (973) 379-7734
chuttner@buddlarner.com
csun@buddlarner.com
bfinkelstein@buddlarner.com

Attorneys for Defendants
Dr. Reddy's Laboratories, Inc. and
Dr. Reddy's Laboratories, Ltd.

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEVADA

AMARIN PHARMA, INC. *et al.*,

Plaintiffs,

v.

WEST-WARD PHARMACEUTICALS CORP., *et al.*,

Defendants.

Case No.: 2:16-cv-02525-MMD-NJK

(Consolidated with 2:16-cv-02562-MMD-NJK, 2:16-cv-02658-MMD-NJK, and 2:17-cv-02641-RFB-GWF)

DEFENDANTS' RESPONSIVE CLAIM CONSTRUCTION BRIEF

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statues

Other Authorities

I. INTRODUCTION

Plaintiffs Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited (collectively, "Amarin") have asserted fourteen patents[1] against the Defendants[2] in this case. The patents all cover a method of lowering triglyceride levels in subjects' blood by administering a pharmaceutical composition containing eicosapentaenoic acid ("EPA"). Thirteen of the patents[3] have the same specification, while the fourteenth patent[4] covers related subject matter. Despite their overlap, Amarin has asserted 224 claims against the Defendants. Because Amarin is asserting this large number of claims, the parties are forced to dispute the meaning of twenty claim terms.

Despite the sheer number of terms, Amarin's claims all suffer from a fatal defect: they are each incredibly specific, drafted as they were in the context of a clinical trial. People had been using EPA—which is found in fish oil—to treat high triglycerides long before the patents-in-suit. To get around this prior art, during prosecution, Amarin relied on a clinical trial it had

---

[1] U.S. Patent Nos. 8,293,728 ("the '728 patent"), 8,318,715 ("the '715 patent"), 8,357,677 ("the '677 patent"), 8,367,652 ("the '652 patent"), 8,377,920 ("the '920 patent"), 8,399,446 ("the '446 patent"), 8,415,335 ("the '335 patent"), 8,426,399 ("the '399 patent"), 8,431,560 ("the '560 patent"), 8,440,650 ("the '650 patent"), 8,518,929 ("the '929 patent"), 8,524,698 ("the '698 patent"), 8,546,372 ("the '372 patent"), and 8,617,594 ("the '594 patent") (collectively, "patents-in-suit") (Plaintiffs' Opening *Markman* Brief ("Amarin's Br.") at Exs. 4-16 [ECF Nos. 89-6 to 89-18]).

[2] Defendants are West-Ward Pharmaceuticals Corp., West-Ward Pharmaceuticals International Limited, Dr. Reddy's Laboratories, Inc., Dr. Reddy's Laboratories, Ltd., and Teva Pharmaceuticals USA, Inc.

[3] The thirteen patents are all continuations of U.S. Patent No. 8,293,727 ("the '727 patent")—a patent listed in the Orange Book for Vascepa, but not asserted in this action—and the '728 patent, the '715 patent, the '677 patent, the '652 patent, the '920 patent, the '446 patent, the '335 patent, the '399 patent, the '560 patent, the '650 patent, the '929 patent, the '698 patent, and the '372 patent (collectively, "the '728 patent family").

[4] The fourteenth patent (*i.e.*, "the '594 patent") is a continuation of U.S. Patent No. 8,298,554 ("the '554 patent")—a patent listed in the Orange Book for Vascepa, but not asserted in this action.

performed, the MARINE trial, and drafted very specific claims reflecting the limitations of the clinical trial. Now, however, in an attempt to accuse Defendants of infringing the patents, Amarin seeks to expand the meaning of the claims to cover situations where a physician simply prescribes medication to a patient. The Court should decline Amarin's attempt to broaden its claims and instead construe the terms in accordance with their plain meaning and the patents' specification.

II. BACKGROUND

Triglycerides and cholesterol are the main lipids or fats found in the circulating blood. (Wharton Decl. ¶25.) Triglycerides and cholesterol are packaged in spherical particles called lipoproteins, which contain both lipids and proteins called apolipoproteins. (*Id*.) Higher levels of triglycerides and bad cholesterol, as well as their corresponding lipoproteins (for example, LDL) and apolipoproteins, are strongly associated with cardiovascular events, including heart attacks. (*Id*. ¶27.) Hyperlipidemia is the medical term for several disorders of lipid metabolism characterized by high levels of triglycerides or cholesterol. (*Id*. ¶30.) Typically doctors treat high levels of triglycerides with lifestyle changes such as diet, exercise, and medication. (*Id*.)

In the 1970s and 1980s, clinical researchers concluded that consuming the omega-3 fatty acids found in fish oils resulted in improved plasma lipid levels in humans. (*Id*. ¶¶31-34.) Practitioners identified omega-3 fatty acids, EPA and docosahexaenoic acid ("DHA"), as the primary active agents in fish oil. (*Id*.) By the early 1990s, it was well-understood that administering fish oil would lower blood triglyceride levels or elevate "good cholesterol," for example, HDL. (*Id*.)

The ethyl ester derivative of EPA—also known as ethyl eicosapentaenoate, icosapent ethyl, ethyl-EPA, or EPA-E—has been commercially marketed since the early 1990s. (*Id*. ¶32.) For example, since 1990, Epadel, a highly purified formulation of EPA-E, has been marketed by

Mochida Pharmaceutical Co., Ltd., in Japan to improve abnormal triglyceride levels. (*Id*.) In 2004 in the United States, the FDA approved the prescription fish oil supplement known as Lovaza (formerly known as Omacor) to treat high triglyceride levels. (*Id*. ¶¶32-33.) Lovaza includes both EPA-E and DHA-E (the ethyl ester of DHA) and is indicated as an adjunct to diet to reduce triglyceride levels in adult patients with triglyceride levels ≥ 500 mg/dl. (*Id*. ¶¶32-33.) However, treatment with Lovaza was known to cause an undesired increase in "bad" LDL cholesterol ("LDL-C"). (*Id*. ¶33.) It was also known that DHA-E, and not EPA-E, was responsible for this undesired effect. (*Id*.)

Since the 1990s, numerous clinical studies conducted on these commercially-available formulations (Epadel and Lovaza) have established the clinical benefits of the administration of a purified formulation containing EPA or its derivatives, namely that EPA-E could reduce triglycerides levels in patients without increasing the levels of undesirable blood lipids, such as LDL-C. (*Id*. ¶34.)

Between 2009 and 2010, Amarin conducted a clinical trial, known as the MARINE trial. (*Id*. ¶35.) The purpose of the MARINE trial was to confirm what was already known in the art—that a pure EPA-E formulation, such as Amarin's formulation, AMR101, lowered fasting triglyceride levels in subjects with fasting triglyceride levels ≥ 500 mg/dl without increasing the level of bad cholesterol like LDL-C. (*Id*.) Amarin used data from the MARINE trial to support FDA approval of AMR101, eventually known as Vascepa, as well as dozens of applications before the U.S. Patent and Trademark Office. (*Id*.) Amarin received approval for Vascepa in 2012 and has marketed its formulation since January 2013. (*Id*.)

III. THE PATENTS-IN-SUIT

Amarin seeks to enforce 224 overlapping claims from fourteen patents against the Defendants. These patents are listed in the FDA's Orange Book in connection with Vascepa. Thirteen of the fourteen asserted patents are entitled "Methods of Treating Hypertriglyceridemia." These patents share identical specifications and claim a method of treating subjects with high triglyceride levels with purified EPA-E, where the measured effects on the subject are compared to the effects on another subject or group.[5] The fourteenth patent, U.S. Patent No. 8,617,594 ("the '594 patent"), is not a member of this family. It is entitled "Stable Pharmaceutical Composition and Methods of Using Same," and has a different specification from the '728 patent family. The '594 patent claims methods of treating one or more subjects in a group of subjects with high triglyceride levels with a pharmaceutical composition containing ultra-pure EPA.

During prosecution of the '728 patent family, the patent Examiner concluded that the claimed methods were obvious. (Amarin's Br. at Ex.[6] 19 [ECF No. 89-27], '728 Patent File History ("PFH"), 4/4/12 Non-Final Office Action at AMRN00212288-99.) Before the Examiner was prior art that taught that administration of pure EPA-E capsules, which also contain substantially no DHA, decreased triglyceride levels in patients. (*Id.*) There was also art that taught that the administration of EPA-E/DHA-E mixtures (*i.e.*, Lovaza) lowered triglyceride levels in patients with triglyceride levels ≥ 500 mg/dl. (*Id.*) Based on these prior art teachings,

[5] For convenience, Defendants will cite here to the '728 patent specification and prosecution history, except where otherwise indicated, to refer to the common specification of all patents but the '594 patent.

[6] Exhibits attached to the declaration of Dr. Michael Miller and the declaration of Megan Keane are referred to as Amarin's Brief Exhibits ("Amarin's Br. at Ex.").

the Examiner concluded that it would be obvious to treat patients having triglycerides levels ≥ 500 mg/dl with a pharmaceutical composition comprising at least about 96% pure EPA-E. (*Id.*)

To overcome the Examiner's finding of obviousness, Amarin attempted to distinguish the prior art by filing a response that included declarations by clinicians and a biostatistician that described the results of Amarin's MARINE clinical trial. (Amarin's Br. at Ex. 19, '728 PFH, 6/27/12 Applicant Response (AMRN00212303-29); Amarin's Br. at Ex. 19, '728 PFH, 6/26/12 Bays Decl. ("Bays Declaration IV") (AMRN00212350-9); Ex. 8, '728 PFH, 5/18/11 Bays Decl. ("Bays Declaration I") (AMRN00212330-32), 12/16/11 Lavin Decl. ("Lavin Declaration I") (AMRN00212366, AMRN00212370-72), 5/10/12 Lavin Decl. ("Lavin Declaration II") (AMRN00212439-43), 5/26/11 Weintraub Decl. ("Weintraub Declaration I") (AMRN00212367-69), and 9/19/11 Weintraub Decl. ("Weintraub Declaration II") (AMRN00212460-68).)[7] The declarations described Amarin's MARINE trial, in which capsules with 4 g of EPA-E (AMR101) were administered for 12 weeks to two groups of hypertriglyceridemic patients: patients who were receiving a concomitant lipid altering medication (first group) and patients who were not receiving a concomitant lipid altering medication (second group). (Amarin's Br. at Ex. 19, '728 PFH, 6/26/12 Bays Decl. (AMRN00212350-59); Ex. 8, '728 PFH, 5/18/11 Bays Decl. (AMRN00212330-32), 5/26/11 Weintraub Decl. (AMRN00212367-69), and 9/19/11 Weintraub Decl. (AMRN00212460-68) submitted with 6/27/12 Applicant Response.) The effect of EPA-E on the triglyceride, cholesterol (*e.g.*, LDL-C and HDL-C), and apolipoprotein B levels of these patient groups was compared with subjects receiving placebo capsules. (*Id.*)

[7] Except for the June 26, 2012 Declaration of Dr. Bays, which was drafted for the '728 patent's application, each of the declarations was first submitted during prosecution of the '727 patent.

Based on the declarations, Amarin argued that the MARINE trial showed that the patients with triglyceride levels ≥ 500 mg/dl who received EPA-E had an unexpected reduction in their apolipoprotein B levels and no change in their LDL-C levels, as compared to Lovaza. (*Id*.) Amarin argued through the declarations that its EPA-E composition fulfilled a long-felt, unresolved need for a treatment that lowered triglyceride levels in patients with triglyceride levels ≥ 500 mg/dl, without an increase in LDL-C. (*Id*.) Even though it was widely known that it was DHA that increased LDL-C and that this effect could be avoided by eliminating DHA from an EPA formulation (for example, Epadel) and the Examiner found that "it will be obvious to treat patients having TG above 500 mg/dl with 96% pure ethyl-EPA," the Examiner nevertheless allowed the claims to issue based on Amarin's unexpected results and long-felt, unmet need arguments. (Amarin's Br. at Ex. 19, '728 PH, 9/6/12 Notice of Allowance at AMRN00212745.)

During prosecution of the '594 patent, Amarin presented arguments similar to those presented during prosecution of the '728 patent, including the unexpected results and long-felt, unmet need arguments. (Ex. 9, '594 PFH, 8/5/13 Applicant Response (AMRN00289323-36).) Again, despite the existing knowledge that pure EPA formulations would not increase LDL-C levels, the Examiner allowed the claims. (Ex. 9, '594 PFH, 9/17/13 Notice of Allowance at AMRN00289713, AMRN00289715.)

IV. THE LEGAL STANDARDS REGARDING CLAIM INTERPRETATION

Claim construction is "of primary importance, in the effort to ascertain precisely what it is that is patented" because "it is 'unjust to the public, as well as an evasion of the law, to construe it in a manner different from the plain import of its terms.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc). Claim construction is the process of determining the scope and meaning of disputed claim terms and is a matter of law exclusively for the Court. *See Markman v. Westview Instruments, Inc. ("Markman I")*, 517 U.S. 370, 372 (1996).

Claim terms "are generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention."[8] *Phillips*, 415 F.3d at 1312-13. There are only two exceptions to this general rule: 1) when a patentee acts as its own lexicographer and redefines a term, and 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution. *See Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012).

In interpreting a claim, one looks first to the intrinsic evidence of record, *i.e.*, the patent itself, including the claims, the specification and, if in evidence, the prosecution history. *See Markman v. Westview Instruments, Inc. ("Markman II")*, 52 F.3d 967 (Fed. Cir. 1995), *aff'd*, *Markman I*, 517 U.S. 370 (1996); *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). "[I]ntrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." *Vitronics*, 90 F.3d at 1582; *see also Phillips*, 415 F.3d at 1317. "[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313. As the single best guide to the meaning of a disputed term, usually the specification is dispositive. *See id.* at 1315.

In construing claims, a court should first "look to the language of the claims to determine what the applicant regards as his invention." *Phillips*, 415 F.3d at 1312 (internal quotations omitted). Terms that appear in more than one claim should be construed consistently throughout the patent. *Id*. at 1314. Moreover, claims and their terms are ordinarily interpreted consistently across patents having the same specification. *See In re Katz Interactive Call Processing Patent Litig.*, 639 F.3d 1303, 1325 (Fed. Cir. 2011) *citing NTP, Inc. v. Research in Motion, Ltd.*, 418

[8] Referred to in this brief by the acronym "POSA."

F.3d 1282, 1293 (Fed. Cir. 2005) ("Because NTP's patents all derive from the same patent application and share many common terms, we must interpret the claims consistently across all asserted patents.").

Further, "[t]he prosecution history gives insight into what the applicant originally claimed as the invention, and often what the applicant gave up in order to meet the Examiner's objections." *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 978 (Fed. Cir. 1999). The Federal Circuit has noted that "[p]rosecution history is an important source of intrinsic evidence in interpreting claims because it is a contemporaneous exchange between the applicant and the examiner." *Desper Prods., Inc. v. QSound Labs, Inc.*, 157 F.3d 1325, 1336-37 (Fed. Cir. 1998). "Arguments and amendments made during the prosecution of a patent application and other aspects of the prosecution history, as well as the specification and other claims, must be examined to determine the meaning of terms in the claims." *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995). A "patentee may not proffer an interpretation for the purposes of litigation that would alter the indisputable public record consisting of the claims, the specification and the prosecution history, and treat the claims as a 'nose of wax.'" *Id.* at 1578 (internal citation omitted). "To act as its own lexicographer, a patentee must clearly set forth a definition of the disputed claim term other than its plain and ordinary meaning." *Thorner*, 669 F.3d at 1365 (internal quotation marks and citation omitted). The patentee must clearly express its intent to redefine the claim term—*i.e.*, the lexicography must be deliberate. *Id.*; *see also Abbott Labs. v. Syntron Bioresearch, Inc.*, 334 F.3d 1343, 1354 (Fed. Cir. 2003). Accordingly, when a general term appears in the claims, a more particularized meaning should not be prescribed unless that narrower construction is required by the specification or the prosecution history. *3M Innovative Props. Co. v. Tredegar Corp.*, 725 F.3d 1315, 1329 (Fed. Cir. 2013).

Moreover, in every instance, extrinsic evidence must be considered "in the context of the intrinsic evidence," and can never be used to "contradict any definition found in or ascertained by a reading of the patent documents." *Phillips*, 415 F.3d at 1319, 1322-23 (internal citation omitted). A court may look to extrinsic evidence to support a claim construction based on the intrinsic evidence, to understand the technology at issue, or to show that a term in the patent has a particular meaning in the relevant field. *See Phillips*, 415 F.3d at 1318; *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S.Ct. 831, 841 (2015).

"A patent must be precise enough to afford clear notice of what is claimed, thereby 'appris[ing] the public of what is still open to them.'" *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120, 2129 (2014) (quoting *Markman I*, 517 U.S. at 373)). The test is whether "a patent's claims, viewed in light of the specification and prosecution history, inform those skilled in the art about the scope of the invention with reasonable certainty." *Nautilus*, 134 S.Ct. at 2129. But the objective of ensuring claims meet "[t]he statutory requirement of particularity and distinctness," remains one of ensuring the claims "clearly distinguish what is claimed from what went before in the art and clearly circumscribe what is foreclosed from future enterprise." *Id.* at 2129 n.6.

V. DISPUTED CLAIM TERMS

During the prosecution of its patents, Amarin made several statements in support of its applications in an attempt to distinguish the considerable amount of prior art available at that time—statements that it now seeks to qualify or minimize to avoid meeting its burden of proof on infringement. Amarin also seeks to escape the other fatal flaw in its claims—that they are written in the context of a clinical study trial. On the other hand, Defendants' constructions stay true to the plain and ordinary meaning of the claims of the patents and seek to hold Amarin to the bargain it struck with the USPTO in obtaining allowance of each of the patents-in-suit.

A. "Concurrent/concomitant lipid altering therapy"

Defendants' Proposed Construction	Amarin's Proposed Construction
any treatment that can cause an alteration in lipid levels whereby such treatment takes place concurrently/concomitantly with the administration of a pharmaceutical composition comprising ethyl eicosapentaenoate	a medication to alter lipid levels in a subject whereby the medication is administered concurrently/concomitantly with the administration of a pharmaceutical composition comprising ethyl eicosapentaenoate
Exemplary claim language ('728 patent, claim 1)	
1. A method of reducing triglycerides in a subject having a fasting baseline triglyceride level of 500 mg/dl to about 1500 mg/dl who does not receive *concurrent lipid altering therapy*…	

The parties' constructions of the term "lipid altering therapy" are similar except with respect to one issue—whether the term is given its proper scope to include all treatments that could alter lipid levels, or whether the term is improperly limited to only medication. Contrary to what Amarin argues, for a number of reasons, the intrinsic and extrinsic evidence does not limit the claimed phrase "lipid altering therapy" only to treatment with medication.

First, as Defendants' expert, Dr. Wharton, explains a POSA would have understood that the plain and ordinary meaning of "lipid altering therapy" includes more than medication. (Wharton Decl. ¶41.) Clinicians routinely prescribe non-medicinal therapy, such as exercise or a change in diet, to patients with elevated triglyceride blood levels to bring down their lipid levels. (*Id.*) Indeed, a POSA usually advises the patient to try both exercise and a change in diet as a first-line therapy to lower their high lipid levels. (*Id.*) If a patient's lipid levels are not lowered with exercise and a change in diet, a POSA may then prescribe medications to be taken alone or concurrently with the lifestyle changes. (*Id.*)

Dr. Wharton's understanding is consistent with the claim language, which recites methods of reducing triglycerides in patients with a certain high, "fasting baseline triglyceride

level." (Amarin's Br. at Ex. 4, '728 patent, claim 1.) A POSA would have understood "baseline" lipid levels to mean an untreated baseline—a lipid level unaffected by any therapy or other factor. (Wharton Decl. ¶46.) In the context of the claims, a POSA would have understood the term "concurrent [concomitant] lipid altering therapy" to include any therapy that "alters" baseline lipid levels. (*Id.*) And because a POSA would prescribe medications as well as changes in one's lifestyle, such as diet and exercise, in order to alter a patient's lipid levels, a POSA would have understood that all such factors, including and beyond medication, are lipid altering therapies. (*Id.* ¶47)

Second, contrary to Amarin's assertion, the specifications of the patents-in-suit do not limit "therapy" to medication. (*Id.* ¶42.) In fact, the specification uses different words to describe lipid altering *medication* and the broader "lipid altering *therapy*." (*Id.* ¶43; *compare, e.g.*, Amarin's Br. at Ex. 4, '728 patent at 13:56-60 with 13:66-14:5). Further, the specification confirms that diet and exercise are *therapeutic* for patients with elevated triglyceride levels. (Wharton Decl. ¶¶42, 45.) For instance, in the specification's prophetic example, patients were required to undergo a "diet and lifestyle stabilization period," implying that diet and lifestyle changes are factors that alter lipid levels in patients. (*See, e.g.*, Amarin's Br. at Ex. 4, '728 patent at 14:19-32; Wharton Decl. ¶42.) In that same prophetic example, the specification refers to lifestyle changes as "therapeutic," requiring all patients be counseled "regarding the importance of the National Cholesterol Education Program (NCEP) *Therapeutic* Lifestyle Changes (TLC) diet." (*See, e.g.*, Amarin's Br. at Ex. 4, '728 patent at 14:32-41 (emphasis added); Wharton Decl. ¶42.)

Moreover, Amarin's piecemeal recitation of the '728 patent at 12:43-46 as supporting its overly narrow construction takes the statement out of context. (Amarin's Br. [ECF No. 89] at 10.) The full statement reads:

> In *one embodiment*, a subject being treated in accordance with methods of the invention is not otherwise on lipid-altering therapy, *for example* statin, fibrate, niacin and/or ezetimibe therapy.

(Amarin's Br. at Ex. 4, '728 patent at 12:43-46 (emphasis added); Wharton Decl. ¶¶44-45.) For one, this statement explicitly refers only to a single embodiment ("In one embodiment") and limiting the claims to a single preferred embodiment constitutes an improper reading of a limitation from the specification into the claims. *Superguide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004) (a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment). Additionally, the phrase "lipid-altering therapy" as used in the statement in question does not limit "therapy" just to drugs. Instead, it merely gives examples (as emphasized above) of drugs that could constitute lipid altering therapy. Nothing in this section (or any section) of the specification defines "lipid altering therapy" as limited to drug therapy or as excluding non-drug therapy.

Third, during the prosecution of the patents-in-suit, the applicants' own expert declarant specifically defined dietary modification and exercise as "lipid altering therapy" along with medication. (Wharton Decl. ¶48.) The applicants' declarant Dr. Howard Weintraub, a cardiologist with over 30 years' experience, stated to the Examiner that "[i]n patients with very high triglycerides, the initial aim of therapy is to prevent acute pancreatitis through triglyceride lowering. This typically requires dietary modification, weight reduction, increased exercise and a triglyceride lowering medication." (Ex. 8, '728 PFH, 5/26/11 Weintraub Decl. ¶7

(AMRN00212368); *see also* Amarin's Br. at Ex. 19, '728 PFH, 6/27/12 Applicant Response at AMRN00212322.) Thus, the prosecution history of the patents also supports Defendants' construction.

Amarin's other citations to the prosecution histories do not support its construction. (Amarin's Br. at 11-12.) The Examiner's description of twenty-four individuals taking anti-hyperlipidemic drugs from a specific prior art reference as patients who were on "concomitant lipid-altering therapy" is consistent with Defendants' construction that does not exclude medications from "lipid altering therapy." (Wharton Decl. ¶49.) Moreover, Katayama, the prior art reference in question, expressly identifies in Table 4 (*see* Amarin's Br. at 12) that therapies can take a non-drug form (*i.e.*, dietary, exercise, and combination). (Wharton Decl. ¶49; Amarin's Br. at Ex. 19, '728 PFH, Katayama at AMRN00209162.) Katayama further identifies concomitant drugs as *drugs*, not therapies. (Wharton Decl. ¶49.) Indeed, the reference itself states that "dietary and/or exercise *therapy* for hyperlipidemia were conducted as appropriate" during the treatment period for diagnosed patients. (*Id.*; Miller Decl. ¶59; Amarin's Br. at Ex. 19, '728 PFH, Katayama at AMRN00209158 (emphasis added).)

Fourth, extrinsic evidence supports Defendants' construction of these terms. For example, the National Cholesterol Education Program (NCEP) Therapeutic Lifestyle Changes (TLC) that the specification references, (*see* Amarin's Br. at Ex. 4, '728 patent at 14:31-41), counsels "[t]reatment for high LDL cholesterol involved the TLC program and, if needed, drug therapy." (Wharton Decl. ¶50; Ex. 7, NCEP TLC at ICOSAPENT_DFNDTS00015354.) Such extrinsic evidence supports Defendants' argument that treatment for high lipid levels, *i.e.* lipid altering therapy, is not limited to drug products, but rather includes treatment with non-drug therapies—that is, diet, physical activity, and weight management. (Wharton Decl. ¶50; *see also*

Ex. 7 at ICOSAPENT_DFNDTS00015345-46 and ICOSAPENT_DFNDTS00015354; *see also, e.g., id.* at ICOSAPENT_DFNDTS00015360 ("[W]hat you eat greatly affects your blood cholesterol levels . . ."); ICOSAPENT_DFNDTS00015378 ("Lack of physical activity is a major risk factor for heart disease . . . Regular physical activity can help you manage your weight and, in that way, help lower your LDL. It also can help raise HDL and lower triglycerides . . ."); ICOSAPENT_DFNDTS00015384 ("Losing your extra weight reduces these risks and improves your cholesterol and triglyceride levels.").)

The extrinsic evidence that Amarin cites, (*see* Amarin's Br. at 28-29), amounts to documents not referenced in the specification (unlike Defendants' reliance on the NCEP-TLC document) and statements that are contrary to the intrinsic evidence. As such, Amarin's extrinsic evidence, consisting of references to other drug labels and cherry-picked medical literature, is entitled to little or no weight and cannot change the definition made clear in the intrinsic evidence. *Phillips*, 415 F.3d at 1319, 1322-23; Wharton Decl. ¶51.

Amarin should not be permitted to use the claim construction proceedings to rewrite its claims to further its litigation strategy. If the applicants had intended to limit "lipid altering therapy" only to medication, they would have consistently used "lipid altering *medication*" throughout, instead of the broader phrase "lipid altering *therapy*," but it did not.

B. "[Orally] administering/administered"

Defendants' Proposed Construction	**Amarin's Proposed Construction**
delivering/delivered into the body [or mouth]	No construction necessary Plain and Ordinary Meaning
Exemplary claim language ('728 patent, claim 1)	

> 1. A method of reducing triglycerides in a subject having a fasting baseline triglyceride level of 500 mg/dl to about 1500 mg/dl who does not receive concurrent lipid altering therapy comprising: *administering orally* to the subject about 4 g per day of a pharmaceutical composition…

Defendants' construction of this term is consistent with the plain and ordinary meaning of "[orally] administering" and "[orally] administered" and defines it as the delivery of the medication in question into the body, such as by the mouth. In contrast, Amarin argues that these terms do not require any construction, stating that "[orally] administering/administered" should be construed to have its plain and ordinary meaning. Having said that, Amarin then proceeds to expand the construction of "administering" to include "prescribing," "instructing," and "treating." By doing so, Amarin seeks to avoid meeting its burden of proof that the Defendants, who are pharmaceutical companies that do not treat patients, meet this claim limitation. Regardless, and contrary to what Amarin argues, based on the context of the word in the claim and when read in light of the specification, a POSA would not broaden the definition of "administering" to the clinicians' "treatment, instruction, or prescribing" actions. A POSA would understand that those actions are distinct from "administering" and would stand on their own.

The intrinsic evidence supports Defendants' construction. The claims are directed to a method of reducing triglycerides and changes to other lipid levels in a subject. There would be no decrease in triglyceride levels or changes to other lipid levels if the subject did not take the medication, *i.e.*, the medication was not delivered into the body.

The specification supports this reading of the claim, disclosing, for example, that

> compositions useful in accordance with methods of the invention are orally deliverable. The terms "orally deliverable" and "oral administration" herein include *any form of delivery* of a therapeutic agent or a composition thereof to a subject *wherein the agent or composition is placed in the mouth of the subject*, whether or not the agent or composition is swallowed. Thus "oral administration" includes buccal and sublingual as well as esophageal administration.

(Amarin's Br. at Ex. 4, '728 patent at 12:47-56) (emphasis added). The specification states that "administration" means "delivery" into the body; and that for "oral administration" even if not swallowed, the agent still enters the body by absorption through the buccal (cheek), under the tongue or throat linings.

Amarin attempts to deceive the Court by truncating the above citation in footnote 12 of its brief, failing to include the final sentence of the paragraph—to assert that delivery into the body is not required and administration can be merely "prescribing" or "instructing." (*See* Amarin's Br. at 15 n.12.) Ending the excerpt with the phrase "whether or not the agent is swallowed" improperly distorts the definition, because the very next sentence that Amarin does not cite in its brief makes clear that even when not swallowed, the agent enters the body through other ways. Contrary to Amarin's proposed definition, the specification is clear in its definition that in all described instances, the drug enters the body. Such a reading makes sense as a requirement to obtain and measure the claimed effect.

The specification also uses the words "treatment," "treating," and "being treated," distinctly (*see, e.g.*, Amarin's Br. at Ex. 4, '728 patent at 8:28-42): if the applicants had intended "administering" to encompass "treating," they would not have differentiated between the two in the specification.

There is ample case law that supports Defendants' construction. In *Takeda Pharm. Co. Ltd., et al. v. Actavis Labs. FL, Inc.*, the Court construed "administering" to mean "delivering into the body," further explaining "[b]eing proceeded by the modifier 'orally' highlights the fact that administering, as used in claim 11 of the '195 patent, refers to the physical means of delivering the medication into the patient's body." C.A. No. 15-cv-451, 2016 WL 3193188, at *2-3 (D. Del. Jun. 6, 2016). The Court in *Pernix Ireland Pain Ltd v. Actavis Labs. FL, Inc.*,

similarly construed "administering" to mean "delivering into the body." C.A. No. 16-138 (GMS), 2017 WL 3314005, at *1 (D. Del. Aug. 3, 2017). *See also Med. Research Inst. v. Bio-Engineered Supplements & Nutrition, Inc.*, C.A. No. 605-cv-417, 2007 WL 128937, at *7 (E.D. Tex. Jan. 12, 2007) ("administer/administration" means "delivering the formulation-in-question into a person's body"); *Sanofi-Aventis U.S. LLC v. Fresenius Kabi USA, LLC*, C.A. No. 14-8079, 2016 WL 5898627, at *6-8 (D.N.J. Oct. 7, 2016) ("administering" means "delivering into the body of a patient" and is distinct from a physician's determination of the protocol for administering the drug).

The cases that Amarin cites in its brief do not support its construction. In fact, in those cases the courts rejected a broad reading of the term "administering," such as the one Amarin attempts to advance here. In *GlaxoSmithKline LLC v. Glenmark Pharms. Inc.*, GlaxoSmithKline, the patent owner, argued that "administering" should be construed broadly to mean "prescribing, dispensing, giving, or taking" without requiring actual delivery to the patient's body. No. 14-cv-877, 2016 WL 3186657, at *15 (D. Del. June 3, 2016). The claims of the patent in *GlaxoSmithKline* were directed to "[a] method of decreasing mortality caused by congestive heart failure." *Id.* at *16. The court noted that "one cannot accomplish this goal for a patient if the patient does not actually take the drugs at issue into her body." *Id.* at *17. The court construed the term to require "what is prescribed, dispensed, given or taken [to be] actually taken into a patient's body." *Id.* Like in *GlaxoSmithKline*, in this case, a subject must, at a minimum, actually take the medication in question into the body. In *Erfindergemeinschaft Uropep GbR v. Eli Lilly and Co.*, the Court rejected Lilly's proposal, identical to Amarin's proposal here, that the term "administering" needed no construction beyond its plain and ordinary meaning as understood by a POSA. 2016 WL 7042234 (E.D. Tex. August 11, 2016). Further,

Erfindergemeinschaft is inapposite because the issue there was whether a pharmacist "administers" the medicine that the pharmacy dispenses. Nonetheless, the court's construction in *Erfindergemeinschaft* fails to support Amarin's broad interpretation. *Id.* at *3. The court warned that construing the term too broadly to include "'giving,' 'providing,' or 'dispensing' would lead one to conclude that a person is 'administering' a drug simply by conveying or providing the drug to another." *Id.* The court concluded that "administering" requires "providing treatment" such that treatment is actually carried out "to ameliorate the issue." *Id.* at *4. In this case, carrying out the treatment would not be possible without the actual delivery of the drug into the patients' body. Additionally, neither of these cases had patents that included the express definition of administration requiring delivery of the medicament into the body found here in the patents-in-suit. (*See* Amarin's Br. at Ex. 4, '728 patent, 12:47-56.)

Finally, because Defendants' construction of "administering" is clearly supported by the intrinsic record, no extrinsic evidence is necessary to support that "administering/administered" means "delivering/delivered into the body [or mouth]." *Intel Corp. v. VIA Techs., Inc.*, 319 F.3d 1357, 1367 (Fed. Cir. 2003) (citing *Vitronics*, 90 F.3d at 1584). Amarin's reliance on extrinsic evidence that expands the definition of "administer" to include only prescribing or instruction without delivery into the body, however, again fails as it is contrary to an express definition for "administration" requiring delivery into the body as stated in the patent specification.

C. "Pharmaceutical composition"

Defendants' Proposed Construction	**Amarin's Proposed Construction**
drug dosage form for administration	a composition suitable for inclusion in a dosage form for administration to patients
Exemplary claim language ('728 patent, claim 1)	

> 1. A method of reducing triglycerides in a subject having a fasting baseline triglyceride level… comprising: administering orally to the subject about 4 g per day of a *pharmaceutical composition* comprising at least about 96%, by weight of all fatty acids present, ethyl eicosapentaenoate, and substantially no docosahexaenoic acid or its esters…

The term "pharmaceutical composition" must be construed as the drug dosage form that the subject takes for treatment and not, as Amarin proposes, simply the active ingredient to be included in the final dosage form. Amarin's construction would improperly capture all drug dosage forms that include 4 g of the active ingredient regardless of the weight of the drug dosage form. But this is not what Amarin bargained for when it prosecuted its patents.

Defendants' construction directly follows from the plain language of the claims which require "administering orally to the subject about 4 g per day of a pharmaceutical composition" to reduce or lower a subject's triglyceride level. (Amarin's Br. at Ex. 4, '728 patent at 16:52-18:44.) A person of ordinary skill in the art would understand this language to pertain to the final drug dosage form, such as a capsule or a tablet, that contains the active ingredient, EPA-E because it is the final dosage form that is administered to the subject, not the active ingredient.

Ignoring this plain language, Amarin simply states, without support, that "[o]nly the weight of the active composition (EPA-E composition) not the surrounding capsule, is relevant to clinical practice." (Amarin's Br. at 19.) It is this statement, however, that is irrelevant. The plain words of the claim specify that the "pharmaceutical composition" is administered to the subject. The subject, into whose body the pharmaceutical composition is being delivered, does not swallow the active ingredient, rather, he or she swallows a finished dosage form like a capsule or tablet.

Defendants' construction of "pharmaceutical composition" is also supported by the specification of the '728 patent, which defines "dosage unit" and "dose unit" as a "portion of a pharmaceutical composition *that contains an amount of a therapeutic agent* suitable for a single

administration to provide a therapeutic effect." (Amarin's Br. at Ex. 4, '728 patent at 12:57-62 (emphasis added).) A POSA reading this statement in the specification would understand that "pharmaceutical composition" is different than a "therapeutic agent" (such as EPA-E).

The language of other claims is also consistent with Defendants' understanding of "pharmaceutical composition." Certain asserted claims specify that the "dosage units are capsules," *i.e.*, a drug dosage form that is administered to the subject. (Amarin's Br. at Ex. 14, '929 patent, claim 9; Amarin's Br. at Ex. 15, '698 patent, claim 8; Amarin's Br. at Ex. 16, '372 patent, claim 25; Amarin's Br. at Ex. 17, '594 patent, claims 9 and 26.) [9] The specification also states that the pharmaceutical "composition . . . is packaged together with instructions for using the composition to treat a cardiovascular disorder." (Amarin's Br. at Ex. 4, '728 patent at 13:20-22.) Similarly, the specification of the '594 patent states that the "compositions of the invention are packaged in blister packs." (Amarin's Br. at Ex. 17, '594 patent at 17:22-23.) Thus, according to the specification, a "pharmaceutical composition" is a drug dosage form, such as a capsule, that is packaged with instructions to patients or doctors on its use and that the patient administers for treatment.

The sole clinical study provided as an example in the specification also confirms Defendants' construction of "pharmaceutical composition." The specification states that the "primary objective of the study" was to "determine the efficacy of AMR101 2 g daily and 4 g daily, compared to placebo" in certain patient populations. (Amarin's Br. at Ex. 4, '728 patent at 13:29-34.) In the clinical study, patients were administered 2 or 4 capsules containing EPA-E

[9] This aligns with the plain meaning of a "dosage unit" in the art. For example, the U.S. Food and Drug Administration uses the term "dosage unit" for the final drug dosage form, such as a tablet, that is administered to a patient in a single administration. *See, e.g.*, 21 C.F.R. §§ 201.64, 201.70, 201.71 (exemplifying a dosage unit by a tablet).

(AMR101), further supporting Defendants' position that the 2 g and 4 g contemplated by the patentee is in the form of the final dosage form, in this case a "liquid-filled, oblong, gelatin capsule." (*Id*. at 15:18-20.) Similarly, the sole pharmaceutical composition, refered to as the "Test Composition," that is prepared and tested in the '594 patent is a capsule. (Amarin's Br. at Ex. 17, '594 patent at 23:18-25:34.)

Finally, the prosecution history supports Defendants' construction. For example, during prosecution of the '728 patent, the applicants argued that the claimed pharmaceutical composition had unexpected results and met a long-felt, unmet need by comparing EPA-E capsules with other drug dosage forms, such as Lovaza; the applicants did not compare the fillings or active ingredients. (*See* Amarin's Br. at Ex. 19, '728 PFH, 6/27/12 Applicant Response at AMRN00212317-28.)

Amarin argues that certain dependent claims in the patent which describe the pharmaceutical composition as being "present in" the capsule differentiate the capsule from the pharmaceutical composition. (Amarin's Br. at 19.) But in fact, these claims, when read in the context of the independent claims and the specification, simply clarify that the pharmaceutical composition can be in the form of a capsule. Other sections of the specification where the pharmaceutical composition is described as "the composition that is present in the capsule shell," would be read by a person of skill as explaining that the composition with the capsule shell is considered a pharmaceutical composition. At best, the sections of the specification that Amarin points to support Defendants' construction, at worst they are inconsistent with the other uses of "pharmaceutical composition" in the patent and the definition of "dosage unit" in the specification. Amarin now cannot rely on its inconsistent usage of the claim term to get its

construction. *Trustees of Columbia Univ. in City of New York v. Symantec Corp.*, 811 F.3d 1359, 1366 (Fed. Cir. 2016).

As with the claim term "concurrent lipid altering therapy," Amarin must live with the language it chose to claim its alleged invention, rather than use claim construction as an opportunity to rewrite its claims. If Amarin wanted to, it could have used the language it used in several other asserted claims to define the amount of active ingredient being administered. (*See, e.g.*, Amarin's Br. at Ex. 15, '698 patent, claim 1 (reciting "a pharmaceutical composition comprising about 4 g of ethyl eicosapentaenoate and not more than about 4% docosahexaenoic acid or its esters, by weight of all fatty acids")[10]; Amarin's Br. at Ex. 4, '728 patent, claims 1, 8, and 19 ("a pharmaceutical composition comprising at least about 96%, by weight of all fatty

[10] *See also* Amarin's Br. at Ex. 9, '446 patent, claim 1 ("administering . . . to the subject 4 capsules per day, each capsule comprising about 900 mg to about 1 g of ethyl eicosapentaenoate and not more than about 3% docosahexaenoic acid or its esters, by weight of all fatty acids"); Amarin's Br. at Ex. 12, '560 patent, claims 1 and 11 ("administering to the subject . . . a pharmaceutical composition comprising about 4 g of ethyl eicosapentaenoate and not more than about 3% docosahexaenoic acid or its esters, by weight of total fatty acids"); Amarin's Br. at Ex. 14, '929 patent, claim 1 ("administering to the subject . . . a pharmaceutical composition comprising about 4 g of ethyl eicosapentaenoate and not more than about 4% docosahexaenoic acid or its esters, by weight of all fatty acids"); Amarin's Br. at Ex. 16, '372 patent, claims 1 and 10 ("administering . . . to at least one subject . . . a pharmaceutical composition comprising about 4 g of ethyl eicosapentaenoate and not more than about 4% docosahexaenoic acid or its esters, by weight of all fatty acids," "administering . . . to at least one subject . . . four capsules per day, each capsule comprising about 900 mg to about 1 g of ethyl eicosapentaenoate and not more than about 4% docosahexaenoic acid or its esters, by weight of all fatty acids"); Amarin's Br. at Ex. 17, '594 patent, claims 1, 10, 17 ("administering . . . to at least one subject . . . about 2500 mg to about 5000 mg of ethyl eicosapentaenoate, present in one or more capsules," "administering . . . to at least one subject . . . 4 capsules, each capsule comprising about 900 mg to about 1 g of ethyl eicosapentaenoate," and "administering . . . to at least one subject . . . about 4 g of fatty acids, at least about 90% by weight of which are ethyl eicosapentaenoate").

acids present, ethyl eicosapentaenoate")[11].) But Amarin chose to use different language in its claim for "pharmaceutical composition" and is bound by it.

Finally, Amarin's extrinsic evidence is irrelevant and should be given no weight. The extrinsic evidence cited by Amarin consists of the U.S. Pharmacopeia and the product list published by a company, Uni-Caps, LLC, that describes the active ingredients in terms of their weight. (Amarin's Br. at 20.) But Amarin fails to explain the relevance these publications have on the claims of the patents at issue. Amarin used certain language to claim its alleged invention and now must be held to the natural construction of those terms.

D. The "Effect Steps": "without effecting a . . . ," "to effect [a] . . . ," "effective to . . . ," "exhibits [a] . . .," "effects [a] . . ."

Defendants' Proposed Construction	Amarin's Proposed Construction
Claim limitation and not merely a statement of intended result or effect. Plain and ordinary meaning	Claim limitation encompassing the intentional purpose for which the method must be performed. Plain and ordinary meaning applies.
Exemplary claim language ('728 patent, claim 1)	
1. A method of reducing triglycerides in a subject…comprising: administering orally to the subject about 4 g per day of a pharmaceutical composition…for a period of 12 weeks *to effect a* reduction in triglycerides without substantially increasing LDL-C compared to a second subject…	

Amarin drafted most of its claims to include functional limitations that recite the effects of administering EPA-E on the lipid levels of subjects receiving the drug. These functional limitations are prefaced by language such as "without effecting a . . .," "to effect [a] . . .," "effective to . . .," "exhibits [a] . . .," and "effects [a] . . ." (the "Effect Steps").

[11] *See also* Amarin's Br. at Ex. 6, '677 patent, claim 1; Amarin's Br. at Ex. 7, '652 patent, claims 1 and 10; Amarin's Br. at Ex. 8, '920 patent, claim 1; Amarin's Br. at Ex. 11, '399 patent, claim 1; Amarin's Br. at Ex. 13, '650 patent, claims 1 and 8.

There is no dispute that the Effect Steps are material to patentability. Rather, Defendants contend that the claimed lipid effects must actually be observed in the subject(s) receiving the drug, whereas Amarin argues that it is sufficient that the physician prescribing the drug subjectively intends that these effects be achieved. But, during prosecution, Amarin argued that the Effect Steps were claim limitations and that conferring specific effects is the objective of the invention. (Amarin's Br., Ex. 19, '728 PFH, 6/27/12 Applicant Response at AMRN00212315 ("Applicant respectfully requests that the requirement for a reduction or no increase in the various lipid parameters be evaluated and accorded patentable weight.").) So while Amarin argued that conferring the specific effect was a required limitation during prosecution to avoid the prior art, it now seeks to avoid its burden of proof on infringement on that element by arguing that "subjective intent" by a clinician would satisfy that requirement.

Amarin's argument is not supported by the intrinsic evidence. As a threshold matter, Amarin's proposed construction would render most of the asserted claims patentably indistinguishable from one another. If the Court were to adopt Amarin's proposed construction, Amarin would escape having to prove these claim limitations for purposes of establishing infringement. There is a strong presumption that dependent claims which include the Effect Steps contain limitations that are not found in the independent claims. *See Phillips*, 415 F.3d at 1315. This presumption demolishes Amarin's argument that the Effect Steps are merely expressions of intended use. Indeed, if this argument were adopted, then most of the asserted claims would be patentably indistinguishable from one another. For example, claim 5 of the '728 patent depends from claim 1. The only additional limitation in claim 5 of the '728 patent is "to effect a reduction in fasting non-HDL-C and a reduction in fasting VLDL-C compared to the second subject." Similarly, the only additional limitation of claim 6 of the '728 patent is "to

effect a reduction in fasting triglycerides of at least about 25% compared to the second subject." The only additional limitation of claim 7 of the '677 patent is "to effect a reduction in fasting triglycerides of at least about 25% without substantially increasing LDL-C compared to placebo control." These exemplary claims would all be rendered redundant (and unpatentable under the doctrine of same invention double patenting, (*see* 35 U.S.C. § 101; *see also, e.g., Miller v. Eagle Mfg. Co.*, 151 U.S. 186, 197 (1894); *In re Vogel*, 422 F.2d 438, 441 (C.C.P.A. 1970)), if the Effect Steps are not considered to require observation of the claimed effect by the person practicing the method of treatment and are instead considered only to require the abstract intent to confer the specific effects.

Additionally, the embodiments described in the specifications of the '728 patent family discuss various treatment outcomes of administering EPA and describe how to observe and measure those outcomes. (Wharton Decl. ¶63; Amarin's Br. at Ex. 4, '728 patent at 8:3-25.) This is most evident in the 12-week study to evaluate the safety and efficacy of AMR101, which describes how the effects of administering EPA are to be measured, compared, and observed. (Wharton Decl. ¶63; Amarin's Br. at Ex. 4, '728 patent at 13:25-14:50.)

Amarin's argument that the Effect Steps require only that the clinician have the abstract *intent* to confer the claimed effects is also not supported by the case law cited in its brief. *Vizio, Inc. v. Int'l Trade Comm'n* dealt with construction of language in the claims' *preamble*. And, the court in that case found that the preamble term "for decoding" was "not merely a statement of purpose or intended use for the invention" but rather "an essential limitation to the claims." 605 F.3d 1330, 1340-41 (Fed. Cir. 2010). *Manning v. Paradis*, 296 F.3d 1098, 1102-04 (Fed. Cir. 2002) dealt with construction of the preamble method of "treating a subject in cardiac arrest" and concluded that the claim term "require[d] a treatment that has a physiological effect on the

subject's heart . . ." *Id.* at 1104. In *Griffin v. Bertina*, the Federal Circuit rejected the argument that the disputed "wherein" clause "merely state[s] the inherent result of performing the manipulative steps." 285 F.3d 1029, 1033-34 (Fed. Cir. 2002). The Court found that "the allegedly inherent properties of the 'wherein' clauses provide the necessary purpose to the steps of obtaining test nucleic acid from a 'test subject' and 'assaying' that material." *Id.*

Amarin's argument that the Effect Steps require only that the clinician have the abstract *intent* to confer the claimed effects, conflicts with the intrinsic evidence described above. Finding the Effect Steps repeatedly recited throughout the specification and asserted claims, the POSA would have considered them to require actual measurement and observation, for the Effect Steps to be meaningful limitations. And Amarin implicitly admits in its Opening Brief that the recited lipid effects must actually occur by stating that claims reciting no increase in LDL-C would not be infringed if there is "any increase in LDL-C value." (Amarin's Br. at 32.)

Further, Amarin's construction is contradicted by the prosecution history of the patents where the applicants unambiguously defined the effect steps as requiring observation of the effect to distinguish the pending claims from the prior art. For example, during prosecution of the '728 patent, the Examiner rejected all pending claims of the application in view of prior art. (Amarin's Br. at Ex. 19, '728 PFH, 4/4/12 Non-Final Office Action at AMRN00212293-5, AMRN00212297-9.) The Examiner explained that the "thereby to" and "wherein" clauses setting forth the effects of administering the pharmaceutical composition merely expressed intended results, and were not entitled to patentable weight. (*Id.*)

In reply, the applicants submitted a Response including an entire section entitled, "The Claimed Lipid Parameters Should be Accorded Patentable Weight," disagreeing with the Examiner and stating that, *inter alia*, the pending claims were amended to recite "effect" in order

to make the claims allowable. (Amarin's Br. at Ex. 19, '728 PFH, 6/27/12 Applicant Response at AMRN00212311-12.) Specifically, the applicants stated:

> Applicant has amended the claims, where appropriate, to remove reference to the term "wherein" or "thereby" and to ***positively recite*** that the pharmaceutical composition, when administered, ***effects a reduction*** in a particular lipid parameter (e.g., triglycerides) or ***does not effect an increase*** in other lipid parameters (e.g., LDL-C).

(*Id*. at AMRN00212311 (emphasis added); *see also* Ex. 10, '715 PFH, 6/27/12 Applicant Response (AMRN00219137-52).)

As Amarin notes in its Opening Brief, [Amarin's Br. at 23], the applicants also relied on *Astrazeneca AB. v. Dr. Reddy's Labs., Ltd.*, C.A. No. 05-5553 (JAP), 2010 WL 11414548 (D.N.J. May 17, 2010), in responding to the Examiner's rejection. The claim in *AstraZeneca* included the phrase "so as to effect decreased interindividual variation in plasma levels (AUC) during treatment of gastric acid related diseases." The plaintiff had proposed "so as to effect" to mean "to bring about," while the defendant had argued that the limitation was "the observed inherent result of the claimed method." (*See* Amarin's Br. at Ex. 19, '728 PFH, 6/27/12 Applicant Response at AMRN00212311 (citing *AstraZeneca*, 2010 WL 11414548, at *9-10).) The court stated:

> [I]n the instant case, the disputed claim terms express the invention of the claimed compound at the high optical purity levels claimed. These are, for example, the unexpected and improved effects of administration of the claimed compound on individuals . . .

AstraZeneca, 2010 WL 11414548, at *10. The applicants endorsed the *AstraZeneca* decision, explaining to the Examiner during prosecution of the patents-in-suit that the *AstraZeneca* "claim language indeed ***required the unexpected and improved effects*** of administration of the claimed compound and therefore was a claim limitation that required construction." (Amarin's Br. at Ex. 19, '728 PFH, at AMRN00212311-12 (citing *Astrazeneca*, 2010 WL 11414548, at *9) (emphasis

added).)[12] So too here, the prosecution histories demonstrate that the applicants for the patents-in-suit intended for the lipid effects recited in the Effect Steps to be material to patentability.

The applicants also submitted multiple declarations during prosecution to establish the importance and unexpectedness of the Effect Steps. These declarations cited heavily to the results of the MARINE clinical trial, the sole embodiment supporting all the claims, specifically, showing observed and measured reduced triglyceride levels, reduced VLDL-C and total cholesterol, and reduced apoB levels. The Examiner allowed the patents relying on these clinically observed results. (Amarin's Br. at Ex. 19, '728 patent PFH, 9/6/12 Notice of Allowance at AMRN00212745-9.)[13] In other words, the applicants' alleged evidence of the clinical effects of EPA-E (albeit, effects that were already known in the art) were found relevant to patentability in large part because the claims required observation of the Effect Steps.

In light of the intrinsic evidence described above, to show infringement, Amarin is obliged to prove that practitioners of the method *actually* measure and achieve the claimed effects, *e.g.*, reduce triglycerides without increasing LDL-C compared to a subject not receiving the pharmaceutical composition.

---

[12] Amarin relies on one sentence from the Court's *AstraZeneca* decision, which Amarin takes significantly out of context. The Court, was discussing prior case law in which "whereby" and "wherein" clauses were found to be claim limitations. *AstraZeneca*, 2010 WL 11414548, at *10-*11. Contrary to Amarin's suggestion, the applicants did not rely on this sentence in their arguments to the Examiner. And, as discussed above, the *AstraZeneca* Court found that the claims required observation of the unexpected and improved effects.

[13] (*See also* Ex. 10, '715 PFH, 6/26/12 Notice of Allowance (AMRN00219257-67); Ex. 11, '677 PFH, 11/8/12 Notice of Allowance (AMRN00225700-07); Ex. 12, '652 PFH, 11/9/12 Notice of Allowance; Ex. 13, '920 PFH, 12/4/12 Notice of Allowance; Ex. 14, '446 PFH, 12/18/12 Notice of Allowance; Ex. 15, '335 PFH, 1/3/13 Notice of Allowance; Ex. 16, '399 PFH, 1/30/13 Notice of Allowance; Ex. 17, '560 PFH, 2/26/13 Notice of Allowance; Ex. 18, '650 PFH, 2/22/13 Notice of Allowance; Ex. 19, '929 PFH, 5/24/13 Notice of Allowance; Ex. 20, '698 PFH, 5/24/13 Notice of Allowance; Ex. 21, '372 PFH, 7/7/13 Notice of Allowance; Ex. 9, '594 PFH, 9/17/13 Notice of Allowance (AMRN00289707-17).)

E. "Compared to . . ."

Defendants' Proposed Construction	Amarin's Proposed Construction
Claim limitation and not merely a statement of intended result Plain and ordinary meaning	Plain and Ordinary Meaning
Exemplary claim language ('728 patent, claim 1)	
1. A method of reducing triglycerides in a subject…comprising: administering orally to the subject about 4 g per day of a pharmaceutical composition…for a period of 12 weeks to effect a reduction in triglycerides without substantially increasing LDL-C *compared to* a second subject having a fasting baseline triglyceride level…	

The plain and ordinary meaning of "compared to" requires the practitioner of the method to make a comparison between subjects or groups, such that the clinical effects may be observed and measured. Amarin argues, however, that construction is not necessary and that the plain and ordinary meaning of "compared to" means that the claimed effect can be compared to "the *expectation* if the subject did not receive purified ethyl-EPA, as described *in the specification, prosecution history, and available clinical trial results.*" (Amarin's Br. at 26.) Amarin's argument is nothing more than an attempt to read the "compared to" limitation out of the claims for purposes of establishing infringement. Under Amarin's construction, a skilled artisan may simply prescribe the pharmaceutical composition to one subject, then compare the effect of that drug to an "intended lipid effect" or an "expectation" of what would have happened if that subject had not received the drug. Amarin's reading of the claims is contrary to the plain language of the claims, the specifications, and statements Amarin made during the prosecution of its patents.

In a number of the asserted claims, the Effect Steps recite administering EPA-E to effect a reduction, or without effecting an increase, "compared to" the lipid parameters measured at baseline or in a placebo or control group. The concepts of reduction and increase have no

meaning if only one measurement is taken, or if no comparison is made. In order to observe, for example, the claimed reduction of triglycerides, or the accompanying absence of increased LDL-C, the practitioner of the method must perform a comparison to effects observed in another subject or population. If the essential comparison is not performed by the person practicing the method of treatment, then there is no infringement under *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S.Ct. 2111 (2014).

The specification discloses that the person practicing the method of treatment makes a comparison. The exemplary embodiment of the MARINE trial, as summarized in the Examples section of the specifications, discloses essential comparison steps to be performed by the practitioner while practicing the disclosed method.

> A multi-center, placebo-controlled randomized, double-blind, 12-week study with an open-label extension is performed to evaluate the efficacy and safety of AMR101 in patients with fasting triglyceride levels ≧500 mg/dL. **The primary objective of the study is to determine the efficacy of AMR101 2 g daily and 4 g daily, compared to placebo**, in lowering fasting TG levels in patients with fasting TG levels ≧500 mg/dL and ≦1500 mg/dL (≧5.65 mmol/L and ≧16.94 mmol/L).
>
> * * *
>
> The primary efficacy variable will be the percent change in fasting TG levels from baseline to Week 12. A sample size of 69 completed patients per treatment group will provide 90% power **to detect a difference of 30% between AMR101 and placebo in percent change from baseline in fasting TG levels, assuming a standard deviation of 45% in TG measurements and a significance level of p<0.01**. To accommodate a 15% drop-out rate from randomization to completion of the double-blind treatment period, a total of 240 randomized patients is planned (80 patients per treatment group).

(Amarin's Br. at Ex. 4, '728 patent at 13:26-34, 16:41-50 (emphasis added).) As disclosed in this specification, the primary objective of the exemplary method is to compare the efficacy of EPA-E with a placebo. (Wharton Decl. ¶63; Amarin's Br. at Ex. 4, '728 patent at 13:29-34.) The practitioner accomplishes this objective by considering at least four measured values—*i.e.*, the

lipid parameters of at least one subject who is administered AMR101 both before and after a treatment period, and the lipid parameters of a control subject both before and after the treatment period. (Amarin's Br. at Ex. 4, '728 patent at 15:34-36; Wharton Decl. ¶63.) As discussed above, the claims reciting that administration of EPA effects a change in lipid parameters are enabled by this exemplary method, and were drafted to capture it.

F. The "LDL-C Terms"

Terms[14]	**Defendants' Proposed Construction**	**Amarin's Proposed Construction**
without substantially increasing LDL-C	Terms are indefinite under 35 U.S.C. § 112.	without a clinically meaningful increase in LDL-C
without effecting a statistically significant increase in LDL-C		without bringing about a rise in LDL-C attributable to the treatment rather than to chance
substantially no increase or a reduction in fasting LDL-C		without a clinically meaningful increase in LDL-C
substantially no increase in LDL-C		without a clinically meaningful increase in LDL-C
Exemplary claim language ('728 patent, claim 1)		

[14] Defendants agree with Amarin's construction of the following terms: "without increasing LDL-C" and "without an increase…" As Amarin states in its brief, where the term is followed by a numberical value, for example, "without increasing LDL-C by more than 5% in the subject," (Amarin's Br. at Ex. 12, '560 patent, claim 4), the term means "the increase is no more than 5%." (Amarin's Br. at 32.) Where there is no numerical value after the term, the term means "without any increase in LDL-C levels in the subject" (*Id.*)

> 1. A method of reducing triglycerides in a subject…comprising: administering orally to the subject about 4 g per day of a pharmaceutical composition…for a period of 12 weeks to effect a reduction in triglycerides *without substantially increasing LDL-C* compared to a second subject having a fasting baseline triglyceride level…

1. "without substantially increasing LDL-C," "substantially no increase in LDL-C," and "substantially no increase or a reduction in fasting LDL-C"

When read in the context of the entire claim and the intrinsic evidence, the LDL-C terms, "without substantially increasing LDL-C," "substantially no increase in LDL-C," and "substantially no increase or a reduction in fasting LDL-C," are indefinite. The LDL-C terms fail to inform those of skill in the art, with reasonable certainty, what degree of LDL-C increase in a subject constitutes a "substantial" increase. The specification provides no guidance as to what rises to the level of "substantially." Amarin proposes that "substantially" means "clinically meaningful," but "clinically meaningful" is a subjective judgment that may vary greatly from clinician to clinician and from subject to subject. (Wharton Decl. ¶73.)

The purpose of the definiteness requirement is to afford the public clear notice of what is claimed and distinguish the claimed invention from the prior art. *Nautilus*, 134 S.Ct. 2120. Recognizing that "patent applicants face powerful incentives to inject ambiguity into their claims," the Court in *Nautilus* explained that the definiteness requirement lets the public know what "is still open to them." *Id.* at 2123, 2129. Whereas here, a term of degree is used in a claim, "the court must determine whether the patent provides some standard for measuring that degree." *Biosig Instruments, Inc. v. Nautilus, Inc.*, 783 F.3d 1374, 1378 (Fed. Cir. 2015) (quotation marks omitted); *see also Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1351 (Fed. Cir. 2005) (holding that when a subjective term is used in a claim, "a court must determine whether the patent's specification supplies some standard for measuring the scope of the [term].").

Simply put, "the claims, when read in light of the specification and the prosecution history, must

provide objective boundaries for those of skill in the art." *Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364, 1371 (Fed. Cir. 2014). To determine the proper scope of a claim, a person of skill in the art must know what falls inside the scope of the claim as well as what falls outside of it. *Meds. Co. v. Mylan, Inc.*, 853 F.3d 1296, 1303 (Fed. Cir. 2017) (citing *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993) ("[C]laims . . . [must be] sufficiently precise to permit a potential competitor to determine whether or not he is infringing.")).

The claims with the LDL-C terms, in their simplest form, claim a method of administering a pharmaceutical composition that causes a reduction in triglycerides but without a "substantial increase" in LDL-C. (*See* Amarin's Br. at Ex. 4, '728 patent, claim 1; Wharton Decl. ¶66.) If the subject concurrently receives another lipid-altering therapy, the method of treatment falls outside the claims. (*See* Amarin's Br. at Ex. 4, '728 patent, claim 1; Wharton Decl. ¶66.) But neither the claims nor the specifications of the patents describes the level of increase in LDL-C that would rise to the level of a "substantial increase." (Wharton Decl. ¶67.) There is no clear, objective standard or boundary in the claims or specification defining the degree of LDL-C increase that constitutes a "substantial increase" such that the treatment would fall outside the scope of the claims. (*Id.*) In fact, neither the specification nor the prosecution history provide any guidance or standard of measure for what constitutes a "substantial increase." (*Id.*)

In Amarin's case, the LDL-C terms do not inform a POSA with reasonable certainty what the scope of Amarin's invention is because (1) the specification fails to define the level of LDL-C increase that constitutes a "substantial increase," (2) the prosecution history fails to present proof of delineating the level of LDL-C increase that constitutes a "substantial increase," and (3) Amarin's construction fails to salvage the lack of any intrinsic evidence. Amarin's attempts to

broaden the definition of "substantial" introduce more ambiguity and uncertainty into the meaning of the claim terms and their limits and boundaries.

For a skilled artisan, the only embodiment in the specification describing an outcome of increased LDL-C levels provides no clarity to the subjective claim language. (Wharton Decl. ¶¶68-73.) The specification for that embodiment describes a wide range of increases from "less than 60% increase" to "no increase in LDL-C levels" at all. (Amarin's Br. at Ex. 4, '728 patent at 5:37-40; Wharton Decl. ¶68.) But such an extreme variation in the percentage increase of LDL-C essentially renders a skilled artisan's understanding of "substantial" meaningless. (Wharton Decl. ¶68; *see also Geodynamics, Inc. v. Dynaenergetics U.S., Inc.*, No. 15-CV-1546, 2016 WL 6217181, at *15-16 (E.D. Tex. Oct. 25, 2016) (rejecting as ambiguous and uncertain the argument that "substantially equal" includes values that are within 35% of equality).) For a clinician, depending on the patient, the treatment of an individual with high triglycerides that results in a 60% increase in the patient's LDL-C level might have very different treatment implications compared to a patient with a 5% increase in LDL-C level since clinicians treat each patient differently. (Wharton Decl. ¶68.) Depending on the particular clinician and the particular patient, certain rises in LDL-C levels may lead to treatment with additional lipid-lowering drugs or the use of an LDL-C lowering drug, rendering the method of treatment of the patents outside the claims of the patent. (*Id.* ¶70.) While one clinician may see a 30% increase in LDL-C level for a particular patient as a cause for prescribing a concurrent lipid-altering therapy, a different clinician may require a higher change in LDL-C level before doing so for the same patient. (*Id.*) Each clinician has different standards for treatment for each patient depending on a patient's family history, lifestyle, age, and other factors. (*Id.*) Thus, to a skilled artisan, the specification's broad range of possible increases in LDL-C provides no meaningful guidance; it only serves to

add ambiguity and uncertainty to the understanding of the claims. *Interval Licensing*, 766 F.3d 1364, 1371 (finding the term "unobtrusive manner" indefinite because the specification and prosecution history failed to provide meaningful guidance to a POSA); Wharton Decl. ¶¶68-73.

There is no other section of the specification that provides an objective boundary to the LDL-C terms. The sole clinical study described in the specification describes a percent change in LDL particle number and size as a secondary efficacy variable of the clinical study, but does not provide any information on the percent change. (Amarin's Br. at Ex. 4, '728 patent at 15:34-53; Wharton Decl. ¶68.) Thus, there is no intrinsic evidence that would allow a POSA to determine the boundaries for the change in a subject's LDL-C values that would render the change "substantial" such that the method of treatment would fall outside the scope of the claims.

Next, the lack of boundary or limit to the LDL-C terms is particularly significant given that Amarin used the LDL-C terms during prosecution to distinguish the subject matter of the invention from the prior art. *Nautilus*, 134 S.Ct. at 2129 n.6 (the definiteness requirement is met when the claims "clearly distinguish what is claimed from what went before in the art"). As Amarin admits, the applicants submitted several declarations during prosecution to argue that, prior to the claimed invention, medications used to lower TG levels often increased LDL-C levels. (Amarin's Br. at Ex. 19, '728 PFH, 6/27/12 Applicant Response at AMRN00212327.) But in every declaration, the applicants failed to provide any guidance as to how much the level of LDL-C in the prior art compositions increased and simply described the increase as "substantial," without further explanation. (*Id.*) Because the applicants used the lack of increase in LDL-C as a factor in distinguishing the invention from the prior art, it stands to reason that a POSA should be able to determine whether a composition raises LDL-C sufficiently enough to

remove it from the scope of the invention. *Meds. Co.*, 853 F.3d at 1303. But the claims and specification do not provide any clarity on the issue.

Amarin's citations to the prosecution history of the patents do not provide any bounds for the LDL-C terms either. Amarin cites to the declarations of the different clinicians it used during prosecution to distinguish the prior art. (Amarin's Br. at 27.) But as explained above, each description of the LDL-C effect on both the prior art and the composition used in the method of the invention fails to describe or outline any set of parameters or boundaries. For example, Dr. Bays explained that the prior art medications increased LDL-C levels and did so "sometimes substantially." (Amarin's Br. at Ex. 19, '728 PFH, 6/26/12 Bays Decl. at AMRN00212357.) Dr. Bays goes on to explain that such an increase was of "clinical consequence," but gives no further explanation as to what degree of increase caused the clinical consequence. (*Id.*)

Amarin's attempt to define the "substantially" terms only doom the terms to greater confusion. (Wharton Decl. ¶73.) Amarin itself does not contend that the bounds of the LDL-C terms can be found in the specification or other intrinsic evidence. (*Id.*) Instead, Amarin proposes a construction that simply substitutes "substantially" with "clinically meaningful," a construction that injects even further ambiguity and uncertainty into the meaning of the claim term. (*Id.*) Amarin's explanation is that a "clinically meaningful" increase in LDL-C is an increase that would require clinical judgment. (*Id.*) Thus, under Amarin's construction, the bounds of the LDL-C terms is within the subjective judgment and range of each individual clinician and would differ among patients. (*Id.*) One seeking to avoid the patent would have no guidance with which to determine whether a prior art composition would raise the LDL-C level in a subject sufficiently enough to remove it from the scope of the invention. Amarin's construction is contrary to established law which states that "a term of degree fails to provide sufficient notice of

its scope if it depends 'on the unpredictable vagaries of one person's opinion.'" *Interval Licensing*, 766 F.3d at 1371 (internal citations omitted).

Amarin's words, without a quantitative objective standard, cannot save the LDL-C terms from rendering the claims indefinite. "Even if a claim term's definition can be reduced to words, the claim is still indefinite if a person of ordinary skill in the art cannot translate the definition into a meaningfully precise claim scope." *Halliburton Energy Servs., Inc. v. M-I LLC*, 514 F.3d 1244, 1251 (Fed. Cir. 2008). In *Halliburton*, the patent owner offered functional construction language to define the term "fragile gel." However, the court rejected the construction because the specification failed to provide any quantitative examples to know the boundaries of what was or was not "fragile."

It is clear that Amarin does not want to limit itself to any limitations to the range of change of LDL-C levels that might be considered a "substantial" increase. *See Nautilus*, 134 S.Ct. at 2129 (prohibiting such unchecked constructions because "absent a meaningful definiteness check . . . patent applicants face powerful incentives to inject ambiguity into their claims"). Amarin's remaining citations to the prosecution history point to statements made by declarants declaring an "extreme 49% increase in LDL-C level" seen in patients treated with Lovaza as being of clinical significance. But, says Amarin, even a smaller 6% increase in the LDL-C level could have clinical significance such that a clinician might consider modifying a patient's treatment regimen. But, Amarin does not conclude that those levels provide the bounds for the LDL-C terms, instead it argues a construction that leaves the term as ambiguous as possible to inappropriately broaden the scope and capture as many products as possible into the scope of the patents.

The cases cited by Amarin are inapplicable and do not support its argument. (Amarin's Br. at 30.) First, both *Deere & Co. v. Bush Hog, LLC,* 703 F.3d 1349 (Fed. Cir. 2012), and *Verve, LLC v. Crane Cams, Inc.*, 311 F.3d 1116 (Fed. Cir. 2002), were decided under a standard for indefiniteness that has been subsequently overruled by the Supreme Court. In *Deere*, the Court found the term "substantially planar" was not "insolubly ambiguous" and was therefore not indefinite. But, in 2014, in *Nautilus, Inc. v. Biosig Instruments, Inc.*, the Supreme Court found the Federal Circuit's "insolubly ambiguous" standard did not satisfy the statutory definiteness requirement and could leave courts and the patent bar "at sea without a reliable compass." 134 S.Ct at 2130.

Further, the *Verve* case, actually supports Defendants argument. In *Verve*, the Court found that words such as "substantially" can be used "when warranted by the nature of the invention, in order to accommodate the minor variations that may be appropriate to secure the invention." 311 F.3d at 1120. The Court explained that such words may serve to describe the invention "with *precision appropriate to the technology* and without intruding on the prior art." (*Id.* (emphasis added).) On both counts, *Verve* counsels in favor of finding the LDL-C terms indefinite. Here, the wide range in LDL-C levels that Amarin suggest may be "substantial" is at odds with the technology of the patent: the treatment of subjects with high triglyceride levels. No person of skill in the art would consider the range of percentage changes of LDL-C between 60% and 6% to be in any way precise. (Wharton Decl. ¶68.) In fact, as Dr. Wharton testifies, such a range of change in LDL-C levels could have a major impact on the health of a patient and would require a significant modification of a patient's treatment. (*Id.*) Further, depending on the change in LDL-C percentage, the composition of the invention could be part of the prior art. As described by Amarin's declarant, Dr. Bays, Lovaza was known to increase LDL-C levels in

patients by 49%, a level he considered "extreme." (Amarin's Br. at Ex. 19, '728 PFH, 6/27/12 Applicant Response at AMRN00212327.) Yet, under Amarin's construction, and the specification of the patent, it remains uncertain as to whether that percentage change is "substantial."

And in *One-E-Way*, the court found the term "virtually free from interference" to mean "the ability to listen without eavesdropping such that a user is not able to listen to another user's transmissions in the wireless digital audio system spectrum." *One-E-Way, Inc. v. Inter'l Trade Comm'n*, 859 F.3d 1059, 1066 (Fed. Cir. 2017). Such clarity with the proposed claim term is not possible here. Reading the claims and under Amarin's construction, a POSA could not, with reasonable certainty, determine unambiguously the limits and boundaries of what constitutes a percentage increase of LDL-C that is a "substantial" increase.

The LDL-C terms do not inform a POSA with reasonable certainty what the scope of Amarin's invention is. In other words, the LDL-C terms inject uncertainty and ambiguity into the claims and fail such that a POSA could not determine whether or not treatment of a subject by a particular pharmaceutical composition fell within the scope of the invention or whether the method of treatment was already known in the prior art.

2. "without effecting a statistically significant increase in LDL-C"

The LDL-C term "without effecting a statistically significant increase in LDL-C" is indefinite for the same reason that the above LDL-C terms are indefinite—it does not inform a skilled artisan with reasonable certainty when an increase in LDL-C rises to the level of "statistical significance."

As with the other LDL-C terms, Amarin's proposed construction injects further uncertainty to a POSA's understanding of this claim term. Amarin's citations to the prosecution

history do not help; they only serve to show that Amarin argued to the Patent Office that the clinical trials for its EPA-E product show no statistically significant changes in LDL-C compared to the prior art product, but Amarin does not explain what the limits and boundaries of the "statistical significance" are.

As Dr. Wharton explains, there can be no statistically significant value for one individual, that term is only used in the context of a group or population of subjects, usually when describing the outcomes of clinical studies. (Wharton Decl. ¶72.) Claims 13 and 14 of the '715 patent, the only claims asserted that contain this claim term, are directed towards a method of treating a subject. Therefore for a POSA, to measure a statistically significant value with respect to one subject, would be impossible. (*Id.*) And even in clinical trials, statistical significance depends on the size of the group and other factors and without more information, a POSA could not determine a statistically significant value with respect to a subject group. (*Id.*)

G. The "Placebo Terms": "placebo control" and "compared to placebo control"

Terms	**Defendants' Proposed Construction**	**Amarin's Proposed Construction**
placebo control	a subject who is administered a placebo and not concurrently administered a pharmaceutical composition comprising ethyl eicosapentanoate	See "compared to placebo control."
compared to placebo control	compared to a subject who is administered a placebo and not concurrently administered a pharmaceutical composition comprising ethyl eicosapentanoate	compared to not administering treatment
Exemplary claim language ('560 patent, claim 11)		

> 11. A method of reducing triglycerides in a subject having a fasting baseline triglyceride level of…comprising, administering orally to the subject… for a period of 12 weeks to effect a reduction in triglycerides in the subject compared to *placebo control*.

Amarin seeks to improperly broaden the scope of the terms "placebo control" and "compared to placebo control" by ignoring the word "placebo." Amarin's construction of "placebo control" would include not only those subjects who are administered a placebo, but also those subjects who are administered nothing at all.[15] Put another way, if the Court were to grant its construction, Amarin would not need to prove that a skilled artisan actually compares two quantified, measured effects (*i.e.*, a placebo versus the active ingredient).

Defendants' proposed construction explains how a POSA would understand the term "placebo control" in the context of the asserted patents. (Wharton Decl. ¶¶74-78; *see also Hockerson-Halberstadt, Inc. v. Converse Inc.*, 183 F.3d 1369, 1374 (Fed. Cir. 1999) ("Proper claim construction . . . demands interpretation of the entire claim in context, not a single element in isolation.").) The claims of the patents-in-suit are directed towards methods embodying a clinical trial. (Wharton Decl. ¶76.) In a clinical trial context, a POSA understands that a "placebo control" is a subject who is administered a placebo and not concurrently administered the studied treatment. (*Id.* ¶75.) Dr. Miller agrees that "[p]lacebo control is a well-understood term in clinical research and evidence-based medicine." (Miller Decl. ¶98; Wharton Decl. ¶76.) Dr. Wharton explains that a POSA would understand that the term "placebo control" requires that a subject receive a pill containing an inactive substance to serve as a standard, a critical element of clinical studies. (Wharton Decl. ¶¶75-76.)

[15] The evidence that supports Defendants' construction of the term "placebo control" also applies to the term "compared to placebo control."

The only description of a placebo in the patents-in-suit is in the context of the MARINE trial where one treatment arm received a matching placebo capsule. (*Id.* ¶¶77-78.) The MARINE trial requires that a subject be administered a placebo and not concurrently be administered a pharmaceutical composition comprising EPA-E:

> A multi-center, **placebo-controlled randomized, double-blind, 12-week study** with an open-label extension is performed to evaluate the efficacy and safety of AMR101 in patients with fasting triglyceride levels ≧500 mg/dL. **The primary objective of the study is to determine the efficacy of AMR101 2 g daily and 4 g daily, compared to placebo**, in lowering fasting TG levels in patients with fasting TG levels ≧500 mg/dL and 1500 mg/dL (≧5.65 mmol/L and ≦16.94 mmol/L).
>
> * * *
>
> After confirmation of qualifying fasting TG values, eligible patients will enter a 12-week, randomized, double-blind treatment period. At Visit 4 (Week 0), **patients will be randomly assigned to 1 of the following treatment groups:**
> AMR101 2 g daily,
> AMR101 4 g daily, or
> **Placebo**.

(Amarin's Br. at Ex. 6, '677 patent at 13:31-39, 14:64-15:3, 15:17-32 (emphasis added).)

The specification then describes the placebo that will be administered to a subject:

> * * *
>
> Eligible patients will be **randomly assigned at Visit 4 (Week 0) to receive orally** AMR101 2 g daily, AMR101 4 g daily, **or placebo for the 12-week double-blind treatment period**. AMR101 is provided in 1 g liquid-filled, oblong, gelatin capsules. **The matching placebo capsule is filled with light liquid paraffin and contains 0 g of AMR101**. During the double-blind treatment period, **patients will take 2 capsules (AMR101 or matching placebo) in the morning and 2 in the evening for a total of 4 capsules per day**. Patients in the AMR101 2 g/day treatment group will receive 1 AMR101 1 g capsule and 1 matching placebo capsule in the morning and in the evening. Patients in the AMR101 4 g/day treatment group will receive 2 AMR101 1 g capsules in the morning and evening.
>
> **Patients in the placebo group will receive 2 matching placebo capsules in the morning and evening**.

(Amarin's Br. at Ex. 6, '677 patent at 13:31-39, 14:64-15:3, 15:17-32 (emphasis added).) The specification unambiguously discusses how the "placebo control" group takes paraffin-filled capsules containing "0 g of AMR101." (Wharton Decl. ¶¶75-76.) Even Amarin acknowledges that this Example requires a comparison to subjects who take a placebo capsule. ("The example in the specification describes a study where the claimed purified EPA-E composition was *compared against a placebo*." (Amarin's Br. at 25 (emphasis added)).)

Yet, Amarin conflates the term "placebo control" with a "control," arguing a POSA would certainly "understand the term 'placebo control' in the claims to be the counterpart to the individual being treated." (Amarin's Br. at 34-35.) But this is incorrect; a "control" is broader in that it describes something that remains the same in an experiment. It could encompass both a subject who is not administered any treatment and a subject who is administered a "sugar pill" (or a paraffin-filled capsule in the MARINE trial Example). (Wharton Decl. ¶¶76-77.)

In fact, Amarin's proposed construction for "placebo control" defeats the design of a double-blind study, such as the MARINE trial. The purpose of a double-blind study is to eliminate observer bias because neither doctors nor subjects know who is receiving the studied therapy. (*Id.* ¶78.) Doctors must administer something that resembles the therapy being tested, *i.e.*, a placebo. (*Id.* ¶76.) Otherwise, both the doctors and the subjects would be aware of who is and who is not receiving treatment. (*Id.* ¶¶76, 78.) In the "placebo-controlled randomized, double-blind" study of the Example, there is no doubt that the placebo group receives a "placebo" in the form of a capsule "filled with light liquid paraffin." (*Id.*) Thus, a POSA would understand "placebo control" to require that a subject be administered a placebo. (*Id.* ¶78.)

Moreover, during prosecution of the patents-in-suit, the applicants submitted multiple prior art references that discuss placebo-controlled studies, where the use of the term "placebo

control" is consistent with Defendants' proposed construction. (Ex. 11, '677 PFH, 10/1/12 Information Disclosure Statement (AMRN00223661-92).)

Amarin offers no support for reading out the term "placebo" from "placebo control" other than the opinion of Dr. Miller, who does not offer any support for his position. (Amarin's Br. at 34-35.) The applicants could have, but did not, use the term "control" instead of "placebo control." Amarin's true intention for its proposed construction is thus to negate the claim language that requires a comparison to placebo control for purposes of establishing infringement.

H. "Identifying a group of subjects"

Defendants' Proposed Construction	**Amarin's Proposed Construction**
identifying a group of two or more subjects	identifying a class of individuals
Exemplary claim language ('372 patent, claim 1)	
1. A method of reducing triglycerides comprising, *identifying a group of subjects* having a median triglyceride level of at least 500 mg/dl . . .	

Amarin does not contest that the "identifying" step in the asserted claims is a material claim limitation. Amarin again, however, attempts to avoid proving infringement on a claim limitation, by proposing a construction that substitutes the requirement that two or more people be identified with the requirement that a hypothetical class of people with similar characteristics, (such as a class of people with severely elevated TG) be identified. (*See* Amarin's Br. at 36.) Amarin does this by changing the language of the claim from its plain and ordinary meaning to something different, changing the words "group" and "subjects" to "class" and "individuals," respectively. (Wharton Decl. ¶80.) Defendants, on the other hand, simply clarify that the claim word "subjects" is plural—"two or more subjects."

Amarin's proposed construction is wrong because the meaning of "group of subjects" is clear from the intrinsic evidence and the applicants did not act as their own lexicographers to

redefine it to mean a "class of individuals." In the description of the clinical study protocol in the patents-in-suit, the specification uses the words "subjects" or "patients" several times and not "individuals." (*Id.* ¶¶85-87.) In addition, there are no references to a "class" in these excerpts or anywhere else in the specification. (*Id.* ¶82.) Without that clear expression of intent to depart from the plain and ordinary meaning of a word, Amarin cannot show that the applicants acted as their own lexicographers to define "group" to mean "class." *See Thorner*, 669 F.3d at 1365.

Amarin's proposed construction is also wrong because construing "subjects" to mean "individuals" is contrary to how a person of ordinary skill in the art would understand the term "subjects." (Wharton Decl. ¶83.) "Subjects" to a POSA, in the context of the patents-in-suit, means people who are participating in an efficacy clinical study, like the clinical study described in the patent specification, that are suffering from a diseased state—such as patients. (*Id.*) "Individuals" on the other hand, is any person—not necessarily someone in a diseased state. (*Id.*)

A POSA would have plainly understood that "identifying a group of subjects" means requiring the identification of more than one subject based on the use of the term "group" and the use of the plural form of the word "subject." (*Id.* ¶84.) A POSA would have also understood that the "identifying" step is to be performed by the person practicing the claimed method. (*Id.*)

I. "Patient population"

Defendants' Proposed Construction	**Amarin's Proposed Construction**
group of two or more patients	a class of subjects
Exemplary claim language ('728 patent, claim 19)	
19. A method of lowering triglycerides…comprising: administering orally to the subject about 4 g per day of a pharmaceutical composition…that is effective to reduce in a first *patient population* receiving 4 g per day of said composition without concurrent lipid altering therapy…	

The proper construction of the phrase as would be understood by a POSA based on the plain and ordinary meaning is "a group of two or more patients." (Wharton Decl. ¶89.) A POSA would have understood that "population," in the context of the patent specification, is being used synonymously with "group," as it would be in normal parlance. (*Id.*) There is no reason to depart from this plain and ordinary meaning to introduce the concept of a "class of subjects" as Amarin improperly proposes. As with the terms above, Amarin's construction seeks to obviate an action that the claims require. Here, the claims require that a skilled artisan compare the actual and measured effects of the pharmaceutical composition to an actual group of patients. Under Amarin's construction, the skilled artisan would simply need to understand the effects that the pharmaceutical composition was known to have in a particular set of patients, for example, patients with high triglycerides.

The intrinsic evidence also does not support Amarin's construction. As explained above, the specification never once uses the word "class" whether referring to patients or subjects. (*Id.* ¶90.) With respect to "patients," the specification and file history talk specifically about *groups* of patients: "patients will be randomly assigned to 1 of the following treatment groups," (*Id.*; Amarin's Br. at Ex. 4, '728 patent at 14:61-67; *see also* 15:15-33, 16:38-50), and "patients are classified into three different groups," (Wharton Decl. ¶90; Amarin's Br. at Ex. 19, '728 PFH, 9/6/12 Notice of Allowance at AMRN00212744.)

VI. CONCLUSION

For the foregoing reasons, Defendants respectfully request that the Court adopt their proposed claim constructions.

Dated: December 12, 2017

Respectfully submitted,

/s/ Alan B. Clement
WAYNE A. SHAFFER (SBN 1519)
LAXALT & NOMURA, LTD.
9600 Gateway Drive
Reno, Nevada 89521
Tel: 775-322-1170
Fax: 775-322-1865
wshaffer@laxalt-nomura.com

ALAN B. CLEMENT (admitted *pro hac vice*)
LOCKE LORD LLP
Brookfield Place
200 Vesey Street, 20th Floor.
New York, New York 10281
Tel.: 212-415-8600
Fax: 212-303-2754
aclement@lockelord.com

MYOKA KIM GOODIN (admitted *pro hac vice*)
JENNIFER CORONEL (admitted *pro hac vice*)
LOCKE LORD LLP
111 S. Wacker Drive
Chicago, Illinois 60606
Tel: 312-443-0700
Fax: 312-443-0336
mkgoodin@lockelord.com
jennifer.coronel@lockelord.com

Attorneys for Defendants
West-Ward Pharmaceuticals Corp. and
West-Ward Pharmaceuticals International Limited

/s/ J.C. Rozendaal
JOHN P. DESMOND
Nevada Bar No. 5618
BRIAN R. IRVINE
Nevada Bar No. 7758
DICKINSON WRIGHT PLLC
100 West Liberty St., Suite 940
Reno, Nevada 89501
Tel: (775) 343-7500
Fax: (775) 786-0131
jdesmond@dickinsonwright.com
birvine@dickinsonwright.com

J.C. ROZENDAAL (admitted *pro hac vice*)
MICHAEL E. JOFFRE (admitted *pro hac vice*)
CHANDRIKA VIRA (admitted *pro hac vice*)
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue N.W.
Washington, D.C. 20005-3934
Tel: (202) 371-2600
Fax: (202) 371-2540
jcrozendaal@skgf.com
mjoffre@skgf.com
cvira@skgf.com

Attorneys for Defendant
Teva Pharmaceuticals USA, Inc.

/s/ Constance S. Huttner

MICHAEL D. ROUNDS, Bar No. 4734
RYAN J. CUDNIK, Bar No. 12948
BROWNSTEIN HYATT FARBER SCHRECK, LLP
5371 Kietzke Lane
Reno, Nevada 89511
Tel: (775) 324-4100
Fax: (775) 333-8171
mrounds@bhfs.com
rcudnik@bhfs.com

CONSTANCE S. HUTTNER (admitted *pro hac vice*)
CAROLINE SUN (admitted *pro hac vice*)
BETH FINKELSTEIN (admitted *pro hac vice*)
BUDD LARNER, P.C.
150 John F. Kennedy Parkway
Short Hills, New Jersey 07078
Tel: (973) 379-4800
Fax: (973) 379-7734
chuttner@buddlarner.com
csun@buddlarner.com
bfinkelstein@buddlarner.com

Attorneys for Defendants
Dr. Reddy's Laboratories, Inc. and
Dr. Reddy's Laboratories, Ltd.

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that I electronically transmitted a true and correct copy of the foregoing **DEFENDANTS' RESPONSIVE CLAIM CONSTRUCTION BRIEF** to the following counsel of record for Plaintiffs in this matter through the Court's CM/ECF efiling program:

Nicholas J. Santoro, Esq. Jason D. Smith, Esq. SANTORO WHITMIRE, LTD. 10100 W. Charleston Boulevard, Suite 250 Las Vegas, NV 89135	Christopher N. Sipes, Esq. Einar Stole, Esq. Michael N. Kennedy, Esq. Megan P. Keane, Esq. COVINGTON & BURLING LLP One CityCenter, 850 Tenth Street NW Washington, DC 20001
Megan Patricia Keane Michael Kennedy Christopher Neil Sipes Einar Stole COVINGTON & BURLING LLP 850 10th Street NW Washington, DC 20001	Jason D Smith SANTORO WHITMIRE 10100 W. Charelston Blvd., Suite 250 Las Vegas, NV 89135
Alan Clement LOCKE LORD LLP Brookfield Place 200 Vesey Street, 20th Floor New York, NY 10281	Jennifer Marie Coronel Myoka Kim Goodin Nina Vachhani LOCKE LORD LLP 111 S. Wacker Dr Chicago, IL 60606
Wayne A Shaffer LAXALT & NOMURA, LTD 9600 Gateway Dr Reno, NV 89521	Maria M Mercera PISANELLI BICE PLLC 400 South 7th Street, Suite 300 Las Vegas, NV 89101
J	

Beth Finkelstein Constance S. Huttner Caroline Sun BUDD LARNER PC 150 John F. Kennedy Parkway Short Hills, NJ 07078	Michael D. Rounds Ryan James Cudnik BROWNSTEIN HYATT FARBER SCHRECK, LLP 5371 Kietzke Lane Reno, NV 89511

DATED this 12th day of December, 2017.

/s/ Cindy S. Grinstead
An Employee of Dickinson Wright PLLC

RENO 74376-2 25565v1